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REMARKS

The specification has been amended editorially to correct spelling and tense errors and claims 14-23 have been rewritten as new claims 24-37 to more particularly define the invention in a patentable manner over the cited prior art.

Specification Amendments

Applicant corrects spelling errors as well as text errors in the present patent application by enclosing with this amendment a clean as well as a marked up version of the specification. The marked up version as well as a clean version are presented since the spelling error occurs throughout the patent application.

The claims rejection under 35 USC 112.

The claims 14-23 were objected to under 35 USC 112 as lacking enablement for a method to prevent a condition of lowered S-adenosyl-l-methionine tissue and blood levels. Applicant agrees with Examiner and withdraws the claims for prevention. Applicant has submitted new claims

The claims rejection under 35 USC 103

The claims 14-19 and 21-23 were objected to under 35 USC 103 as being unpatentable over Gennari US 4, 465, 672 and De La Cruz et al Naunyn-Schmiedeberg's Archives Pharmacology (2000), pages 47-52.

P. 37 (blank)

Applicant submits along with this amendment, a declaration under rule 132 to address technical points regarding the non-obviousness of Applicant's invention. Briefly stated here:

1. S-adenosyl-l-methionine is a diastereomer consisting of 2 important stereoisomers, (S,S) S-adenosyl-l-methionine and (R,S) S-adenosyl-l-methionine.
2. S-adenosyl-l-methionine is epimerically unstable in powder form and at room temperature. (S,S) S-adenosyl-l-methionine form, the important biological stereoisomer, epimerizes to its (R,S) S-adenosyl-l-methionine form which inhibits the very reaction that makes the (S,S) S-adenosyl-l-methionine an important fundamental biologically active molecule.
3. There is no mention in prior art (with exception of Berna patent application) of epimeric instability of (S,S) S-adenosyl-l-methionine in the powder form on the shelf. (Berna patent application discussed in declaration.) No prior art teaches methods of use of substantially optically pure (S,S) S-adenosyl-l-methionine salts. (Berna patent only teaches a process for making S-adenosyl-l-methionine.) Applicant is first to realize the importance of substantially optically pure (S,S) S-adenosyl-l-methionine for clinical use and first to teach methods for the use of substantially optically pure S-adenosyl-l-methionine for the treatment of conditions as stated in Applicant's pending patent application.

Comments on conditions claimed for which (S,S) S-adenosyl-l-methionine is beneficial.

New claim 29 cites the following conditions that can be treated with (S,S) S-adenosyl-l-methionine: DNA and RNA hypomethylation, inflammation, ageing, Alzheimer's disease, osteoarthritis, rheumatoid arthritis, cancer, depression, chronic liver disease, alcohol liver disease, cirrhosis of the liver, strokes, Parkinson's disease, impaired memory, HIV dementia, auto-immune diseases, and parenteral nutrition induced liver disease.

It is understandable that one would be skeptical regarding the number of potential disease states that are treatable using this molecule. However, when one understands the very fundamental role S-adenosyl-l-methionine plays in biological reactions, then its widespread utility can be recognized. By correcting DNA or RNA hypomethylation, for example, one is able to correct and treat a wide variety of cancers since DNA global hypomethylation is a hallmark of cancer. Correcting DNA hypomethylation will silence genes that have been unintentionally turned on.

Thus, the commonality among the conditions listed in the new claim 29 have all an aspect of reduced levels of S-adenosyl-l-methionine and DNA hypomethylation associated with the mechanism of action of S-adenosyl-l-methionine. The mechanism of action of S-adenosyl-l-methionine in osteoarthritis may have to do with its ability to provide sulfur groups to synovial membranes, but it may also have to do with direct anti-inflammatory activity by inhibiting Tumor Necrosis Factor alpha, an important pro-inflammatory cytokine.

In medicine, it would be considered unusual to use an anti-depressant as an anti-inflammatory drug and also use it, for example, to prevent cirrhosis of the liver and its

progression on to hepatocellular carcinoma. That same drug then would be used to treat metastatic cancers that have as their hallmarks, not only global DNA hypomethylation, but also increased urokinase production.

Urokinase is an enzyme abnormally expressed in aggressive metastatic cancers such as breast, colon, prostate and lung. S-adenosyl-l-methionine is able to correct the hypomethylation status of the gene that codes for the urokinase promoter gene thus effectively stopping the production of the urokinase and thus stopping the ability of breast, colon, prostate, lung and perhaps others from metastasizing. Since S-adenosyl-l-methionine is able to silence urokinase genes by correcting the hypomethylation status of its promoter, S-adenosyl-l-methionine could be used to treat conditions associated with increased urokinase levels (that is, conditions unrelated to cancers mentioned.) Thus, urokinase is abnormally elevated in macular degeneration, cardiac fibrosis, and may be implicated in re-stenosis of angioplasties.

The forgoing discussion is meant to underscore the many different conditions in which S-adenosyl-l-methionine may be useful. The reason for its importance is reflected in its participation in the very fundamental activities of animal biology, that is, gene expression, and thus through this very fundamental activity, it influences disparate diseases. The diseases cited in new Claim 29 are conditions known to be associated with low cellular, blood or tissue levels of S-adenosyl-l-methionine.

CONCLUSION

For the above reasons, applicant submits that the claims are now in proper form, and that the claims all define patentably over the prior art. Therefore the Applicant submits that

this application is now in condition for allowance, which action applicant respectfully solicits.

Conditional Request for Constructive Assistance

It is submitted that patentable subject matter is clearly present. If the examiner agrees but does not feel that the present claims are technically adequate, applicant respectfully requests the constructive assistance and suggestions of the examiner pursuant to MPEP 2173.02 and 707.07 (j) in order that the applicant can place this application in allowable condition as soon as possible and without the need for further proceedings.

Very respectfully,

RHebert date 10/18/04

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Certificate of Facsimile Transmission.

I certify that on the date below I will fax this paper (including declaration and Exhibits) to GAU 1623 of the US Patent and Trademark Office at 703-872-9306.

Date RHebert 10/18/04

Rolland Hebert